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(54) **Oximeter apparatus and method for measuring arterial blood constituents.**

(57) An oximeter and method is disclosed for non-invasively measuring blood which is capable of determining the oxygen saturation of arterial blood. The oximeter includes at least one light source addressed to a tissue area of a patient, such as a finger or earlobe. A photodetector receives emitted light passing through the sample and a receiver circuit analyzes the data and produces an output which is proportional to the oxygen content of blood. The light source is driven at a preselected carrier frequency and the receiver circuit is tuned to said carrier frequency so that undesired signals can be filtered out leaving only the signals created by the emitted light passing through said tissue. The oxygen content is calculated using the patient's known red cell count, thereby correcting the final saturation value for patient anemia. Moreover, the calculation for oxygen saturation incorporates red cell scattering parameters for increased accuracy in clinical environments.

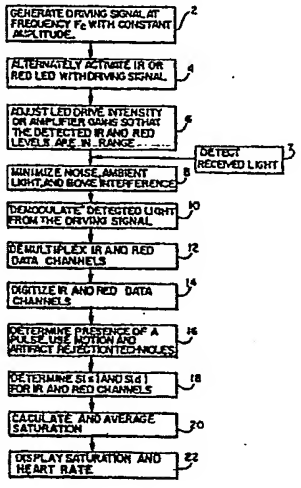

FIG. 1

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Description

OXIMETER APPARATUS AND METHOD FOR MEASURING ARTERIAL BLOOD CONSTITUENTS

Field of the Invention

This invention relates to the field of devices and methods for non-invasively measuring blood constituents which are capable of determining the hemoglobin oxygen saturation of blood and, more particularly, to devices which detect variations in the detected light amplitude of one or more wavelengths which are transmitted through body tissue and which compensate in some manner for ambient light interference.

Background of the Invention

The determination of blood oxygen and other blood constituents such as injected dyes has become a greater interest to physicians and of greater importance in the practice of clinical medicine. Generally, it is known to use spectrophotometric techniques to measure arterial hemoglobin oxygen saturation. Moreover, various blood constituent measuring devices and methods use non-invasive techniques wherein emitted light is passed through the sample, or reflected therefrom, to light sensors. Variations in the detected light at various wavelengths are then used to determine arterial oxygen saturation, and/or pulse rates. Such devices and/or methods are shown, for example, in U.S. Patent Nos. 4,407,290; 4,266,554; 4,167,331; 4,086,915; 3,998,550; and 3,647,299; and European Patent Nos. EP 0 104 771 A3 and EP 0 102 816 A3.

With respect to prior art oximetry devices and methods in particular, significant errors are induced in clinical oximetry if the classical absorption equation (Bier's Law) is used to calculate the saturation of oxygen as applicable to pure hemoglobin. Such methods are disclosed in U.S. Patent Nos. 4,167,331; 3,998,550; 4,086,915; and 4,266,554. Other patents teach the use of a mathematical approximation to Bier's Law by using ratios of the pulsating absorbance and the non-pulsating absorbance components of each of several wavelengths of transmitted light. (See, for example, U.S. Patent Nos. 4,407,290 and 3,647,299; and European Patent Nos. EP 0 104 771 A3 and EP 0 102 816 A3.) Because the light absorption of tissue does not exactly correspond to that predicted by Bier's Law, some type of empirical calibration may be performed as taught in U.S. Patent Nos. 4,407,290; 4,167,331; and 4,086,915.

The technique of deriving the absorbance in the pulsating component is taught in different ways. One technique relies upon the quantitative measurement in the change of absorbance at each wavelength. See, for example, U.S. Patent No. 4,407,290 and European Patent Nos. EP 0 104 771 A3 and EP 0 102 816 A3. It is also known that the derivative of the change in absorbance and a peak to peak measurement of the pulsating absorbance component may be used to calculate the oxygen content of arterial blood. See, for example, in U.S. Patent Nos. 4,407,290 and 4,167,331.

When a single light detector is used, the detected light for each wavelength must be separated. This is accomplished by using time separation and synchronous detection. See, for example, U.S. Patent Nos. 4,407,290; 4,266,554; and 3,647,299. Because the light detectors also detect ambient light, some type of ambient light rejection technique is normally employed. Some patents use four clock states and allow for subtraction of ambient light. See, for example, U.S. Patent Nos. 4,407,290 and 4,266,554. Some patents use techniques to remove the non-pulsating absorbance component since ambient light is usually a non-pulsating absorbance frequency. See, for example, U.S. Patent Nos. 4,167,331 and 3,998,550. These techniques consider light to have a constant amplitude.

Although these techniques and devices have been utilized, they are not completely satisfactory and are deficient in several areas. Bier's Law and/or the use of empiracal estimates usually only approximate the oxygen content of blood in living tissues in clinical environments. Prior techniques for removing ambient light and motion artifacts are unsatisfactory and generally produce decreased signal to noise ratios and increased errors in the clinical measurements because up to fifty percent of the duty cycle is devoted to making ambient light measurements. Techniques using synchronous detectors are not completely satisfactory since they require wide bandwidth AC amplifiers and because they also may devote a significant portion of the duty cycle, as much as 50%, to measuring the ambient light rather than the desired absorbance changes. The wide bandwidth requirements of the prior art devices are more susceptible to frequency interference such as BOVIE interference. BOVIE interference is a type of system noise produced by electrical surgical devices such as coagulators and cauterizers. It typically effects the frequency range of .5 to 5 MHZ, but can be found even in direct current. While there is less energy in frequencies between DC and .5MHZ, there is still enough energy to potentially cause interference which impairs the performance of many prior art devices. Previous embodiments also frequently require an analog channel for each wavelength and require that these channels be matched over the bandwidth. The analog requirements may be so stringent as to require that both channels have a "normalized" DC output. See, for example, U.S. Patent No. 4,407,290.

While blood constituent measuring devices and methods have heretofore been suggested and have achieved some success, a need still exists for more accurately measuring the oxygen saturation of the blood in anemic patients particularly those with blood conditions, such as low red blood cell counts. These blood counts are different from the assumed counts upon which the factory "pre-sets" are based. Correcting for anemia in the saturation equations, for example, could be a critical factor in keeping an anemic's brain and heart alive during surgery. There is also a need for a device which is less sensitive to other types of

interference, such as BOVIE interference, which can virtually interrupt oximetry at critical times during operation.

Summary of the Invention

A novel blood constituent measuring device and method are provided which exhibit an excellent signal to noise ratio and improved resistance to interference from ambient artificial light, and BOVIE interference, etc. This is accomplished by driving one or more light sources with a driving signal. This driving signal, does not exhibit a frequency which is present in the artificial light environment of the operating room. The light transmitted through the body tissue is then received by a receiver means which is tuned to the preselected driving signal to produce a demodulated output. As a result, no portion of the duty cycle must be devoted to measuring ambient light, and the narrow band pass filters employed reduce BOVIE interference.

The present invention also provides novel techniques for determining and displaying pulse and oxygen saturation values. Blood oxygen levels are calculated using equations which include red cell scattering parameters, and measurements may be corrected for abnormal red cell counts. The device also utilizes other novel signal processing techniques, including digital analysis and interpolation of temporally distinct detected light amplitudes.

It is, therefore, an object of this invention to provide a blood constituent measuring device and method.

It is another object of this invention to provide a blood constituent measuring device and method capable of determining the oxygen saturation of arterial blood in relation to the fraction of red blood cells per unit volume of whole blood.

It is still another object of this invention to provide a blood constituent measuring device and method that can provide an output which indicates arterial pulse.

It is still another object of this invention to provide a blood constituent measuring device and method that rejects motion artifacts by subtracting extraneously detected data from a detected pulse data reading.

It is still another object of this invention to provide a blood constituent measuring device and method that calculates the oxygen saturation of arterial blood using red blood cell absorbance and scattering parameters.

With these and other objects in view, which will become apparent to one skilled in the art as the description proceeds, this invention resides in the novel construction, combination, arrangement of parts, and methods substantially as hereinafter described and more particularly defined by the attached claims.

Brief Description of the Drawings

The accompanying drawings illustrate a complete embodiment of the invention according to the best mode so far devised for the practical application of the principles thereof, and in which:

FIG. 1 is a process flow diagram for an oximeter utilizing in this invention;

FIG. 2 is a software flow diagram showing digital to analog conversion points for interfacing with the oximeter's hardware, as well as processing steps for sampling light intensity readings, storing said readings, and calculating saturation values for hemoglobin in patient's blood;

FIG. 3 is a detector block flow diagram indicating the elements of the detector and receiver circuitry and possible locations for adjusting the amplifier gain;

FIG. 4 is a light-emitting diode driver flow diagram indicating how a preferred square wave driving signal is generated, with optional adjustment to drive current and an optional calibration verification procedure;

FIG. 5 is a schematic of the light emitting diode driver circuitry;

FIG. 6 is a schematic of the detector circuitry;

FIG. 7 is an exemplary bar graph, showing a room light spectrum of the estimated amplitudes of interfering ambient artificial light in a hypothetical environment where the power line frequency is a nomal 60 cps; the actual relative amplitudes of such interference and their frequencies varying somewhat depending upon power line frequency, lighting source, etc.

Description of the Invention

The following description is provided to enable any person skilled in the medical and electronic fields to make and use the invention and sets forth the best mode contemplated by the inventor of carrying out his invention. Various modifications, however, will remain steadily apparent to those skilled in the art since the generic principles of the present invention have been defined herein specifically to provide a relatively economical and easily manufactured non-invasive blood constituent measuring device.

The invention herein described includes at least one light source driven with a preselected driving signal, which source is placed in proximity to and directed through a patient's body tissue, a photodetector for receiving the light transmitted through that tissue, and a receiver circuit tuned to the driving frequency of the light source. The device effectively excludes ambient light, and limits BOVIE interference and system noise by driving the light source with a signal having a frequency not found in the ambient light environment. A processing means processes the receiver circuit output and calculates blood saturation using scattering parameters which are proportional to the red cell count in the tissue.

Referring now to the drawings, Figure 1 is a process diagram of an oximeter utilizing the instant invention. A driving signal having a pre-selected waveform is generated at process step 2. The driving signal is used to alternately activate the light emitting diodes at step 4. An adjustment of the light emitting diode drive intensity and/or amplifier gains can be made at step 6, so that the detected light levels 7 are within the range of the

analog to digital converters used in the hardware. Noise, ambient light, and BOVIE interference are then minimized at step 8. The detected light signal is then demodulated from the driving signal at step 10. Demultiplexing the data channels is then accomplished at step 12, and the output of step 12 is digitized at process step 14. The data is then processed by determining the presence of a pulse and implementing motion and artifact rejection techniques at step 16. Saturation values are then calculated for each wavelength of light a step 18, and an average value for saturation is determined at step 20. Finally, the saturation and heart rate values are displayed at step 22.

Referring now to the software flow diagram in Figure 2, the driving signal in step 2 above which preferably has a uniform amplitude and frequency, such as a square or a sine wave, is selected to drive a pair of light emitting diodes at a pre-determined clock state, designated " Φ_1 " or " Φ_2", at software step 30. Adjustments to the diodes' driver current and the oximeter's amplifier gain can be made at steps 32 and 34, respectively. Before data points representing transmitted light values are sampled at step 40, the software enables system transients to settle at step 60. The delay necessary to overcome transients in the waveform during a given clock state will vary according to the wave generating circuit used and the amount of duty cycle required for measuring data points. In the preferred embodiment no more than 25% of the waveform generated by the driver circuit should be used for transient settling. Preferably, less than 10%, and most preferably, less than 5% of the waveforms should be allocated for waiting for transients to settle. Alternatively, the settling time can be terminated when the transient amplitude comprises less than 1%, and preferably less than .1%, of the amplitude of the theoretical waveform. The samples points designated as "M" are then either averaged or filtered by using a digital filter at software step 42. The averaged or filtered data points are then placed into a buffer at software step 44, for enhanced signal to noise ratios and better analog to digital resolution.

Detecting the pulse presence and amplitude in software step 46 is accomplished by first measuring the light intensity readings for the preferred red and infrared wavelengths at software step 48. Values at step 48 may be at peaks or at other times in the cycle, but should be measured or estimated at a synchronous point in time. Since alternate clock states are preferred, an interpolation at step 50 is used for this purpose. By interpolating measured values of the light detected from one light-emitting diode to estimate a detection value when said diode is not illuminated, the device can render the clock states, Φ_1 and Φ_2 synchronous.

An anemia correction calculation is then made at software step 52. The correction for anemia is made by incorporating into the saturation calculations, a factor "η" which is equivalent to the fraction of red cells per unit volumn of whole blood which is calculated from the hemoglobin concentration.

The software process next encompasses calculating the saturation value "S" at sept 54. An average saturation value may be calculated as appropriate at step 56, and the results are displayed at step 58.

Referring next to the detector flow diagram in Figure 3, software step 34 operates to adjust the amplifier gain through the digital to analog converter 68. The gain adjustment is made in the band pass filter element at block 72. This band pass filter receives the output from the linear photo detector of block 70, and operates with the whole wave rectifier, block 74, and envelope detector, block 76, to form an AM demodulator. These hardware elements carry out the process steps of eliminating interference and demodulting the detected light values from the driver frequency, process steps 8 and 10 of Figure 1. A differential amplifier follows next in block 78 which adds both parts of the whole wave rectifier output together. The output of the differential amplifier is then fed into a low pass filter at block 80 which is intended to eliminate ripple from the carrier frequency and generally improve the signal to noise ratio. The preferred embodiment also permits a possible gain adjustment at block 86 to keep the analog signal appropriate for the analog to digital converter, block 82.

Referring next to the driver flow diagram found in Figure 4, a driving signal having a pre-selected waveform, as previously discussed, is generated at block 94 which corresponds to process step 2. The resulting driver waveform can be biased up or down by block 96 to drive back to back LED's. This biasing step may also be replaced by a switching means for alternatively driving each light-emitting diode. It is also noted that software step 30 operates through digital to analog converters 90 and 92 to determine the duration of excitation of the light emitting diodes. Software step 32 also operates on the driver circuit to determine the intensities of the illuminated light emitting diodes in block 100. Block 102 represents an optional calibration verification procedure which can be adapted to this preferred embodiment.

When only one driving signal is used to drive two light- emitting diodes, the light-emitting diodes are driven alternatingly by that signal. The duration of excitation of each light-emitting diode is known as the clock-state and is designated as "T". If two light-emitting diodes are used, two clock-states are selected and are designated as Φ_1 and Φ_2. It is contemplated that the light-emitting diodes can be driven using signals such as decaying waveforms or other coded waveforms. These are not presently preferred since tuning the recurring means to, or decoding, those waveforms is somewhat more complicated. In any event, the driving signal does not substantially overlap with the substantial artificial light amplitudes in the intended location of use.

The light-emitting diodes should be kept as bright as possible to improve the signal to noise ratio of the device. However, at least one light-emitting diode may require adjusting. the light-emitting intensities are intentionally not adjusted to be equal.

Referring next to the light-emitting diode driver schematic found in FIG. 5, a "555" integrated circuit 106 is used to generate a drive frequency. The present configuration produces a uniform square wave at 47kHz. It is desirous that the carrier frequency be as high as possible to optimize settling times of the oximeter's circuitry. However, it may also be desirable to choose frequencies which are located below the frequency of the ambient light or in between the harmonics of the ambient light. As a minimum requirement, "a frequency not

substantially present in the ambient light" means that the frequency is not within an amplitude which comprises greater than 1% of the amplitude of the ambient light. Moreover, "in between frequencies" may be defined as within a range delineated by two principle harmonic frequencies, plus or minus 10% of said harmonic frequencies.

Using the 60 cycle per second frequency found in the power lines of the United States, one could choose a carrier frequency of less than 60 cycles per second, in between the harmonics of this frequency: 120, 240, 480, and 960 cycles per second, or greater than an arbitrary cutoff point of power line harmonic interference. (See figure 7 depicting a hypothetical ambient light spectrum with frequencies of 120,240, 360 and 480 cps.) In the present embodiment, a carrier frequency above the fourth harmonic would ideally avoid most ambient light harmonic interference.

This principle is equally applicable to power line frequencies outside the United States, such as 50 to 55 cycles per second found in Europe. Several examples of selected frequency ranges are herein provided to serve as a reference:

Example 1: Possible ranges for carrier frequencies for a power line frequency of 60 cycles per second.

1. Less than 54 cycles per second.
2. Between 66 and 108 cycles per second.
3. Between 132 and 216 cycles/second.
4. Between 264 and 432 cycles/second.
5. Above 1056 cycles/second.

Example 2: Possible ranges for carrier frequencies for a power line frequency of 50 cycles per second.

1. Less than 45 cycles/second.
2. Between 55 and 90 cycles/second.
3. Between 110 and 180 cycles/second.
4. Between 220 and 360 cycles/second.
5. Above 880 cycles per second.

Example 3: Possible ranges for carrier frequencies for a power line frequency of 55 cycles per second.

1. Less than 49.5 cycles/second.
2. Between 60.5 and 121 cycles/second.
3. Between 121 and 198 cycles/second.
4. Between 242 and 396 cycles/second.
5. Above 968 cycles/second.

Furthermore, in this driver schematic, the voltage at resistor 134 which we will call "V_1" is in the form of a square wave at a fixed carrier frequency with the maximum voltage equal to the voltage across resistor 128 and a minimum voltage equal to 0 volts.

Output from the digital to analog converter 116 is either +10 volts of 0 volts and is used to determine clock states Φ_1, Φ_2 selected at software step 30 in Figure 2. For this embodiment, a Computer Continuum LAB 40 with a LAB 40-2 12-bit analog to digital module is used. Bit 0 of the 8-bit data output is connected to the operational amplifier 124. A summation operation amplifier configuration 144 is used to combine the carrier frequency voltage across resistor 132 with the offset voltage across resistor 130 generated by the digital to analog converter 116. The output voltage at 146 is a square wave with a frequency F_c. At Φ_1, the maximum voltage equals 10 volts, the minimum voltage equals 0 volts or at Φ_2, the maximum voltage equals 0, and the minimum voltage equals -10 volts. A buffer operation amplifier 148 follows.

The light-emitting diode current driver section follows the buffer 148. Power transistors 152 and 158 are used. For this embodiment, transistor 152 is a TIP 31 and transistor 158 is a TIP 32. Load resistors 154 and 156 are used to determine light-emitting diodes 160 and 162 current and brightness.

Generally, the physiology requires that the red light-emitting diode be about twice as bright as the infrared light-emitting diode. Thus, resistor 154 is chosen to deliver about 100mA to the red light-emitting diode and resistor 156 is chosen to deliver about 50mA to the infrared light-emitting diode. Attenuating the infrared light-emitting diode to about 50% yields both intensities near each other at the detector. This is for convenience, and not a requirement. The two light emitting diodes 160 and 162 are connected in opposite directions. Thus, a current driven in one direction will illuminate one of the light-emitting diodes and a current in the opposite direction will illuminate the other, producing a pulsing effect. Since the opposed relationship is not a requirement, this device could also employ separate wirings for each LED.

A later embodiment of this light-emitting driver circuit encompasses a calibration verification device shown by the digital to analog converter 138 and resistor 140. A small sine signal at 1Hz or other suitable waveform, such as one emulating an arterial pulse, would produce a signal which would be interpreted at the detector as a pulse. Resistor 140 could be any value to keep the scale appropriate.

This embodiment also utilized a voltage across resistor 128 of +12 volts. Also included in this embodiment was an adjustment made at rheostat 112 so that the fixed carrier frequency was equal to 47kHz. The operation amplifiers 118, 124, 144 and 148 in this configuration are BiFets, TLØ74 and the light-emitting diodes used in this embodiment are from a Nellcor D-25 Oxisensor. A linear photo-detector 70 of the detector flow diagram Figure 3, is used for detecting the transmitted light from the body tissue of a patient. A linear photo detector is

used so that the output of the photo-detector is directly proportional to the input as represented by the light emission intensities. For this embodiment, the photo detector used is from a Nellcor D-25 Oxisensor. Capacitor 104 is 88 µf. Capacitors 108 is .1µf and 110 is .01 µf. Resistors 120, 122, 126, 134 and 136 are 10KΩ. Resistors 132, 142 are 100 KΩ and 150 is 100Ω. Resistor 114 is 135Ω. Resistor 112 is variable. Resistor 128 is 46 KΩ. Resistor 130 is 220 KΩ. Resistor 140 can be preselected. Resistor 154 is 100 and resistor 156 is 200 .

Referring next to the detector electrical schematic in Figure 6, the photo detector 70 is connected directly to an operation amplifier as represented by diode 164, resistor 166 and operation amplifier of FIG. 6.

The next stage is a band pass filter circuit, 300 and 400, of FIG. 6 designed with a center frequency at the carrier frequency. For this embodiment, two band pass filters were used, 300 and 400. The first band pass filter 300 had a gain equal to 10 and Q equal to 50. The second band pass filter 400 has a gain equal to 4, but variable, and a Q equal to 10. This plurality of band pass filter states enables the oximeter to filter out noise frequencies while at the same time accepting only the frequency associated with the admitted light intensities. This frequency filtering state acts much like a tuner on a radio in that the band pass filters are matched or tuned to the carrier frequency. The use of a narrow bandwidth devices represents a significant improvement over the wide band AC amplifiers of the prior art.

By using a narrow band width amplifier as opposed to a wide band, BOVIE interference, created by electronic surgical instruments which can sufficiently cause interference in a range less than 1kHz, can be minimized. BOVIE interference, which typically effects the frequency range of .5 to 5 mHz; can be found even in direct current. Wide band amplifiers pick up the BOVIE signal more readily, thereby, creating more error in the clinical environment. A narrow band amplifier like the one used herein has a much greater chance at eliminating BOVIE interference and can produce a better signal to noise ratio.

A variable gain direct current inverting amplifier represented by resistor 204 and operation amplifier 206 follows the band pass filter 400 to allow the user to adjust the overall system gain as appropriate to yield an output voltage which is approximately 8 volts for the larger voltage channel.

A calibration adjustment 500 is found in the detector circuitry next. The 3000 pF capacitors 220 and 224 can be removed and voltages on the rectifier 214 are adjusted until equal using this trimpot procedure.

A full wave rectifier 600 follows. Time constants on the envelope detectors located within the full wave rectifier 600 should be less than 1 msec. or less than 10% of "T". This would allow a complete settling time of about 4 msec. or 40% of "T". This allows approximately 60% of "T" for sampling data points. Preferably the time constant is less than 0.25 in sec. or less than 2.5% of "T". This would allow a complete settling time of 1 msec. or 90% of "T". Resistors of 270 KΩ, 222 and 226, and capacitors of 3000 pF, 220 and 224, yield 1 msec. time constant. Additional setting time requirements may be imposed by the low pass filter section 700.

The time constants for the envelope detectors are inversely proportional to amount of ripple from the carrier frequency such that the smaller the time constant, the larger the ripple detected. Although the ripple can be averaged out later, it will affect accuracy of the instrument to some extent.

The ripple (r) is calculated as a function of the driving frequency, the resistance in the envelope detector and the capacitance in the envelope detector. See R.E. Smith, Circuits, Devices, and Systems, Wiley, New York, Second Edition, 1967, p. 429.

The bandpass filter circuit, full wave rectifier, and envelope detectors in combination, operate on the driver wave frequency to recover the waves representing detected light intensity values which were previously modulated with the driving frequency.

A differential amplifer 800 follows which consists of resistors 234, 236, 237, 238, and operational amplifier 240. For this embodiment, the differential amplifier should have matched components; here they are shown as tolerances of 1%.

The low pass filter sections 700 follow. Two identical low pass filters are shown in series. The low pass filter should have a cutoff frequency low enough to reject ripple from the rectifier by at least -100 dB, yet not so low that the higher harmonics of the pulse wave form are rejected. The other requirement is that the rise time or setting time be fast enough, in the same order as the rectifier circuits 600, so that adequate time is available at the end of each clock state for sampling data points.

The minimum settling time filters used in this preferred embodiment are BESSEL filters with damping factors, ζ, equal to 0.8659. A two-pole BESSEL filter is preferred with a cutoff frequency of 250Hz with 98% settling of 1 ms.

The output voltage from the second low pass filter represented by resistor 252, capacitor 256, resistor 254, capacitor 258 and operational amplifier 260 is connected directly to the analog to digital converter 262. For this embodiment, a COMPUTER CONTINUUM LAB 40 with a LAB 40-2 12-bit analog to digital module is used.

The output data from the preferred embodiment circuitry is used to calculate a pulse rate and saturation values. The following variables are used in the software program found herein and summarized in Figure 2:

Φ_1, Φ_2: clock states or periods of excitation of light-emitting diodes;

M: the number of analog to digital conversions or sample data points during a Φ state lasting for T;

T: the duration of a clock state, Φ ;

V_{Ir}: the voltage intensity reading as measured by the photo detector from the infrared light-emitting diode.

V_r: the light intensity reading as measured by the photo detector from the red light-emitting diode;

S[d]: the light intensity measured at diastole and is the virtual incident intensity for pulse oximetry;

S[s]: the light intensity measured at systole ;

S: the fractional oxygen saturation of hemoglobin.

The operating principles of the present invention will now be described. Hemoglobin is actually a concentration of oxyhemoglobin and a concentration of deoxyhemoglobin. Because there are two species present, two different and unique wavelengths of light must be used to generate two simultaneous equations. A minimum of one wavelength is required for the measurement of each separate blood constituent component. These equations which model the extinction of light by clinical oximeters as a function of absorbence and scattering. Since scattering is a function of wavelength, hemoglobin concentration and saturation, including scattering terms decreases the amount of errors which have caused previous oximeters, which relied on absorbence factors, to be inaccurate in certain clinical environments. (See example, Joseph M. Schmitt, Optical Measurement of Blood Oxygen by Implantable Telemetry, 31, 41 (February, 1986), Standard Electronics Laboratories, (describing scattering coefficients in the implantable telemetry art.)

The teaching of the thesis entitled "Optical Measurement of Blood Oxygen by Implantable Telemetry" by Joseph M. Schmitt is relevant to the discussion of calculating oxygen saturation of hemoglobin and is hereby incorporated by reference into this specification.

The general function for the total observed light at an observation point is given by the following equation:

(1) $S(p) = \Psi_o \Sigma_{st} \exp(-\Sigma_t z) R(r)$,

where

$S(p)$ = source function or amount of detected light;

Ψ_o = incident light flux;

$R(r)$ = function describing radial distribution of light beam intensity which is assumed to equal 1 for this discussion.

The more useful saturation determination is arterial hemoglobin saturation. Because at systole there is a rapid inflow of arterial blood, measuring the change in light extinction from late diastole to early systole will facilitate this measurement. These types of oximeters are designated pulse oximeters. For pulse oximetry, S[p] assumes values between S[d], intensity at late diastole, and S[s], intensity at early systole. S[s] corresponds to the intensity measured during systole and is the transmitted intensity for pulse oximetry. S[d] corresponds to the intensity measured at last diastole and is the virtual incident intensity for pulse oximetry. The optical path, or incremental change because of pulsation or the inflow of arterial blood, also changes yielding a value of z′ at diastole and z″ at systole. Then two equations can be written for diastole and systole.

(2) $S(d) = \Psi_o \Sigma_{st} \exp(-\Sigma_t 2')$

(3) $S(s) = \Psi_o \Sigma_{st} \exp(-\Sigma_t z'')$

The difference in extinction between diastole and systole is due primarily to inflow of arterial blood.

(4) $S(d)-S(s) = \Psi_o \Sigma_{st}[\exp(-\Sigma_t z')-\exp(-\Sigma_t z'')]$.

But, z″ equals z′ + z where z is the incremental change due to pulsatile flow. Then the equation can be rewritten as

(5) $S(d)-S(s) = \Psi_o \Sigma_{st}[\exp(-\Sigma_v z')-\exp(-\Sigma_t z')\exp(-\Sigma_t z)]$;

(6) $S(d)-S(s) = \Psi_o \Sigma_{st} \exp(\Sigma_t z')[1-\exp(-\Sigma_t z)]$.

For any invivo transducer application, the terms Ψ_o, Σ_{st}, and $\exp[-\Sigma_t z']$ will be a consant for a particular clinical situation which we will designate as K for now. Then the equation becomes:

(7) $S(d)-S(s) = K[1-\exp(-\Sigma_t z)]$.

Now it becomes necessary to develop the terms of Σ_t.

(8) $S(d)-S(s)/K = [1-\exp(-(\sigma_{ao}S + \sigma_{ar}(1-S) + \Sigma_{st}/\eta)\eta z)]$

(9) $[1-(S(d)-S(s)/K)] = \exp(-(\sigma_{ao}S + \sigma_{ar}(1-S) + \Sigma_{st}/\eta)\eta z)$

In the above equation, only two variables, S and z, are present and the other terms are constants, some being wavelength dependent. The next step is to take logarithms.

(10) $\ln[1-(S(d)-S(s))/K] = (\sigma_{ao}S + \sigma_{ar}(1-S) + \Sigma_{st}/\eta(\eta z$

(11) $-\ln[1-(S(d)-S(s))/K] = (\sigma_{ao}S + \sigma_{ar}(1-S) + \Sigma_{st}/\eta)\eta z$

(12) $-\ln[1-(S(d)-S(s))/K]/\eta z = (\sigma_{ao}S + \sigma_{ar}(1-S) + \Sigma_{st}/\eta)$

(13) $(\sigma_{ar}-\sigma_{ao})S-\ln[1-(S(d)-S(s))/K]/\eta z = \Sigma_{st}/\eta + \sigma_{ar}$

Because there are two variables, two equations or wavelengths are needed.

(14) wavelength 1: $-\ln[1(S_I(d)-S_I(s))/K_I]/\eta z + (\sigma_{arI}-\sigma_{aoI})S = \Sigma_{stI}/\eta + \sigma_{arI}$

(15) wavelength 2: $-\ln[1-(S_{II}(d)-S_{II}(s))/K_{II}]/\eta z + (\sigma_{arII}-\sigma_{aoII})S = \Sigma_{stII}/\eta + \sigma_{arII}$

where

σ_{ao} is equal to absorption cross section of an isolated red cell containing completely oxygenated hemoglobin;

σ_{ar} is equal to absorption cross section of an isolated red cell containing completely deoxygenated hemoglobin;

σ_s is equal to scattering cross section;

μ is equal to an asymmetry parameter;

η is equal to fraction of red cells per unit volume of whole blood;

H is equal to hematocrit fraction of whole blood;

Σ_{st} is equal to modified scattering coefficient of whole blood;

Σ_s is equal to scattering coefficient of whole blood;

Σ_a is equal to absorption coefficient of whole blood;

Σ_t is equal to sum of modified scattering and absorption coefficients of whole blood;

z is equal to distance or curvette length;

Σ_a is equal to $\eta\,[\sigma_{ao}S + \sigma_{ar}(1-S)]$;

Σ_s is equal to $\eta\ \sigma_s(1-H)$;
Σ_{st} is equal to $\Sigma_s(1-\mu)$;
Σ_t is equal to $\Sigma_a + \Sigma_{st}$;
Σ_t is equal to $\eta[\sigma_{ao}S + \sigma_{ar}(1-S)] + \Sigma_{st}$; and
K is equal to constant for the product of the source function, incident light flux, and exp $(-\Sigma\ _{tz})$.

These are two simultaneous equations in variables S and l/z. The four measurements:$S_I[d]$, $S_I[s]$, $S_{II}[d]$ and $S_{II}[s]$ are made. The hemoglobin concentration is used to calculate η. Correcting the concentration formulae for the number of red blood cells per unit volume of whole blood is a novel approach to problems associated with anemia which had been ignored by the prior art. The above equations utilize this important factor to calculate the oxygen content thereby providing a more accurate means to measure blood constituents of anemic patients. The following table is used which displays the other constants needed for two hypothetical wavelengths, 910nm and 660nm.

	910nm	660nm
σ_{ao}	.1340	.0357
σ_{ar}	.0802	.3547
σ_s	36.34	60.65
σ_{st}	.276	.309
μ	.9924	.9949

The variable K includes gain factors, but in particular contains the overall gain factor which will be different for each wavelength channel and will require determination depending upon hardware. Also a unit conversion factor must be included since the variables in K contain physiology and measurement parameters, such as S(d). Thus S(d) and S(s), in whatever units they happen to be must be converted to physiology terms, i.e. the units in the log expression must cancel. Note further K_I and K_{II} are neither equal nor do they render $S_I(d)$ and $S_{II}(d)$ to be equal, or $S_I(s)$ and $S_{II(s)}$ to be equal.

These equations can be solved by methods of linear algebra to determine S. Using techniques of matrix manipulation, a determinate is made and then the calculation of S.

The computer program receives the output signals from the analog to digital converter 262 and calculates the oxygen saturation [S] in the blood according to equations (14) and (15). The operation performing the solving of the selected equations amounts to multiplying, dividing, adding and subtracting utilizing the received variable and the stored constants.

The program used in this preferred embodiment is written in BETTER BASIC [Summit Software Technology, Inc., 1984] and is attached to this specification. The software has interfacing points with the analog hardware at digital to analog converters 1, 2 and 3 of FIG. 2. The program alternates between the two clock states for setting the output latch digital to analog converter 45, to 10 volts or ground, waiting to the end of the state and sampling only one data point [M = 1] 8.

Using an IBM-XT, the program in this preferred embodiment produces a clock state duration, T, of 12ms. 8. A buffer 10 of a thousand data points are taken for the red and the infrared channels. The buffer 44 is recorded onto a disc for examination by the higher level of software calculations 11 through 16.

The processing next encompasses calculating the saturation value S using the equations (14) and (15) as previously discussed. An average saturation 16 may be calculated as appropriate at this point in the processing.

As seen from above, the driving signal used to vary the amplitude of LED output within each clock state is not a clocking signal, i.e. it does not function to alternatively activate two or more LED's. In the present device a second signal produced by the clocking means is superimposed as the driving signal for performing this function. Increases in the frequencies of prior art clocking signals would not accomplish the results disclosed herein because such increases would require the use of extremely wide band amplifiers in the receiver, and thus would not improve, and may decrease, the signal to noise ratio of the device.

The following program writting in BETTER BASIC [Summit Software Technology, Inc., 1984], is used in the preferred embodiment of this invention.

```
PROGS=0
REAL: PA0,PA1,PB,PC,CO,CW,LBYTE,HBYTE
REAL: VALUE,J
REAL ARRAY(1000): RED,IR
REAL: I,X
   10 ' SAMPLE.BAS: 23-AUG-1986: MARK YELDERMAN
   20 ' BETTER BASIC FOR IBM-XT
   30 ' COMPUTER CONTINNUM USING LAB 40-2 A/D CONVERTER, 12 BITS
   40 ' ------------------------------------------------------
   50 '******************************************************
   60 '  Definition of LAB 40 Port addresses
   70 PA0=736:PA1=737
   80 PB=740:PC=744:CO=748
   90 CW = 192 ' CONTROL WORD FOR PORT A BI-DIRECTIONAL AND PORT B OUT
  100 CLS
  110 OUT (CO,CW)    'DEFINE LAB 40 PORT DIRECTIONS
  120 OUT (PC,2)     'SET UP BOARD SELECT 2 TO ENABLE 12 BIT MODULE
  130 ' THE LAB 40 BUS IS NOW READY TO TALK TO THE 12 BIT MODULE
  140 ' NOW TAKE DATA
  150 FOR J=0 TO 999
  160   OUT (PA1,1)    'CHANGE OUTPUT STATE BY STARTING A/D
  170   ' DO MATH FOR PREVIOUS CONVERSION
  180   VALUE = HBYTE*256+LBYTE   ' COMPUTE 12 BIT VALUE
  190   '
  200   RED(J)=VALUE   'RESULTS FOR STATE "0"
  210   FOR I=1 TO 2:X=I:NEXT     'THIS IS A DELAY LOOP
  220   OUT (PA0,1)    'START A/D CONVERSION WITH AN OUTPUT INSTRUCTION
  230   OUT (PB,0)     'SET BYTE SELECT TO READ LOW BYTE
  240   LBYTE=INP(PA0):LBYTE=INP(PA0) ' READ IN LOW BYTE FROM PORT A
  250   OUT (PB,1)     'SET BYTE SELECT TO READ HIGH BYTE
  260   HBYTE=INP(PA0):HBYTE=INP(PA0) ' READ IN HIGH BYTE
  270   '
  280   OUT (PA1,0)    'CHANGE OUTPUT STATE BY STARTING A/D
  290   ' DO MATH FROM PREVIOUS CONVERSION
  300   VALUE = HBYTE*256+LBYTE   ' COMPUTE 12 BIT VALUE
  310   '
  320   IR(J)=VALUE 'RESULTS FOR STATE "1"
  330   FOR I=1 TO 2:X=I:NEXT     'THIS IS A DELAY LOOP
  340   OUT (PA0,0)    'START A/D CONVERSION WITH AN OUTPUT INSTRUCTION
  350   OUT (PB,0)     'SET BYTE SELECT TO READ LOW BYTE
  360   LBYTE=INP(PA0):LBYTE=INP(PA0) ' READ IN LOW BYTE FROM PORT A
  370   OUT (PB,1)     'SET BYTE SELECT TO READ HIGH BYTE
  380   HBYTE=INP(PA0):HBYTE=INP(PA0) ' READ IN HIGH BYTE
  390 NEXT
  400 OPEN "TEST.DAT" FOR OUTPUT AS #2
  410 FOR J=0 TO 999
  420   PRINT #2 USING "####.#  ####.#"; RED(J),IR(J)
  430 NEXT
  440 CLOSE
  450 FOR J=0 TO 99
  460   PRINT USING "####.#  ####.#"; RED(J),IR(J)
  470 NEXT
ENDFILE
```

A list of components which have been utilized in a working embodiment of this invention is set forth hereinafter. It is to be realized, however, that the invention is not meant to be limited to the components as listed. The component list is as follows:

Transistors:	152-TIP 31; 158-TIP 32.
Light-Emitting Diodes:	160 and 162 taken from a NELLCOR D-25 oxisensor.
Linear Photodetector:	taken from a NELLCOR D-25 oxisensor.
Operation Amplifiers:	TL074 BiFets

Resistors: 112-variable; 114-135; 120-10K; 122-10K; 126-10K; 128-46K; 130-220K; 132-100K; 134-10K; 136-10K; 142-100K; 150-100; 154-100; 156-200; 166-470K; 170-15K; 172-100K; 178-33K*; 184-100K; 186-68K; 192-variable; 196-680K; 200-1.5K; 204-200K; 222-270K; 226-270K; 234-10.1K; 236-10.1K; 237-5K; 238-5K; 242-1M; 246-1M; 252-1M; 254-1M.
Capacitors: 104-88uf; 108-.01uf; 110-.01uf; 174-100pf; 180-100pf; 194-100pf; 202-100pf; 208-100pf; 220-3,000pf; 224-57pf; 248-433pf; 256-577pf; 258-433pf.
Driver: 106-555
Digital to Analog Converters--COMPUTER CONTINUIUM LAB 40 with a LAB 40-2 12 Bit A/D Module.

* Variable for gain

From the foregoing it can be realised that this invention provides an improved device and method for blood constituent measurement. The advantages over the prior art are: improved duty cycle, more accurate modeling by using scattering in addition to absorbance parameters, and higher accuracy in the clinical environment by accounting for red blood cell count and by filtering out ambient light, Bovie interference, and system noise. Although apparatus have been illustrated, this was for the purpose of describing, but not limiting, the invention. Various modifications, which will become apparent to one skilled in the art, are within the scope of this invention described in the attached claims.

Claims

1. A blood constituent measuring device for non-invasive measurement of the concentration of a blood constituent, having a light source for transmitting light through a body tissue of a patient and a detector oriented for detecting at least the light transmitted through the patient's body tissue, characterized in that the device includes a driver for providing the light source with a pre-selected driving signal having a frequency not substantially present in the artificial light, receiver for receiving the output of the detector and tuned to said pre-selected driving signal for producing a de-modulated output, and a processor for receiving the de-modulated output from the receiver and for producing at least an output which is proportional to the concentration of the blood constituent.

2. A blood constituent measuring device according to claim 1, characterized in that said processor further comprises apparatus for producing at least an output which is proportional to the oxygen content of the patient's blood.

3. A blood constituent measuring device according to claim 1, characterized in that the frequency of the pre-selected driving signal is greater than the frequency of the fourth harmonic of the frequency of greatest amplitude in the artificial light.

4. A blood constituent measuring device according to claim 1, characterized in that the frequency of the pre-selected driving signal comprises a frequency which is located in-between a pair of harmonics of the artificial light.

5. A blood constituent measuring device according to claim 1, characterized in that the driver is matched to the receiver with respect to the frequency of the pre-selected driving signal for allowing passage of the pre-selected driving signal and rejecting other frequencies.

6. A blood constituent measuring device according to claim 1, characterized in that the receiver comprises a filter for allowing passage of the pre-selected driving signal and for rejecting other frequencies.

7. A blood constituent measuring device according to claim 1, characterized in that the processor comprises apparatus for generating a correction signal which is proportional to the fraction of red blood cells per unit volume of whole blood and for correcting for an altered extinction of light due to scattering which is proportional to a reduced blood cell count.

8. A method for non-invasively measuring the concentration of a blood constituent for use in an environment generally illuminated by artificial light including the steps of providing light for transmission through a body tissue of a patient and detecting at least the light transmitted through the patient's body tissue, characterized in that the method further includes the steps of driving the light with a pre-selected driving signal having a frequency not substantially present in the artificial light, receiving the output of the detecting step, wherein the receiving step tunes into the pre-selected driving signal and produces a demodulated output, and processing the demodulated output to produce at least an output which is proportional to the blood constituent.

9. A method for non-invasively measuring the concentration of a blood constituent according to claim 1, characterized in that the processing step produces at least an output which is proportional to the oxygen

content of blood.

10. A method for non-invasively measuring the concentration of a blood constituent according to claim 8, characterized in that the processing step further comprises generating a correction signal which is proportional to the fraction of red blood cells per unit volume of whole blood and correcting for increased extinction of light due to scattering of light which is proportional to a reduced blood cell count.

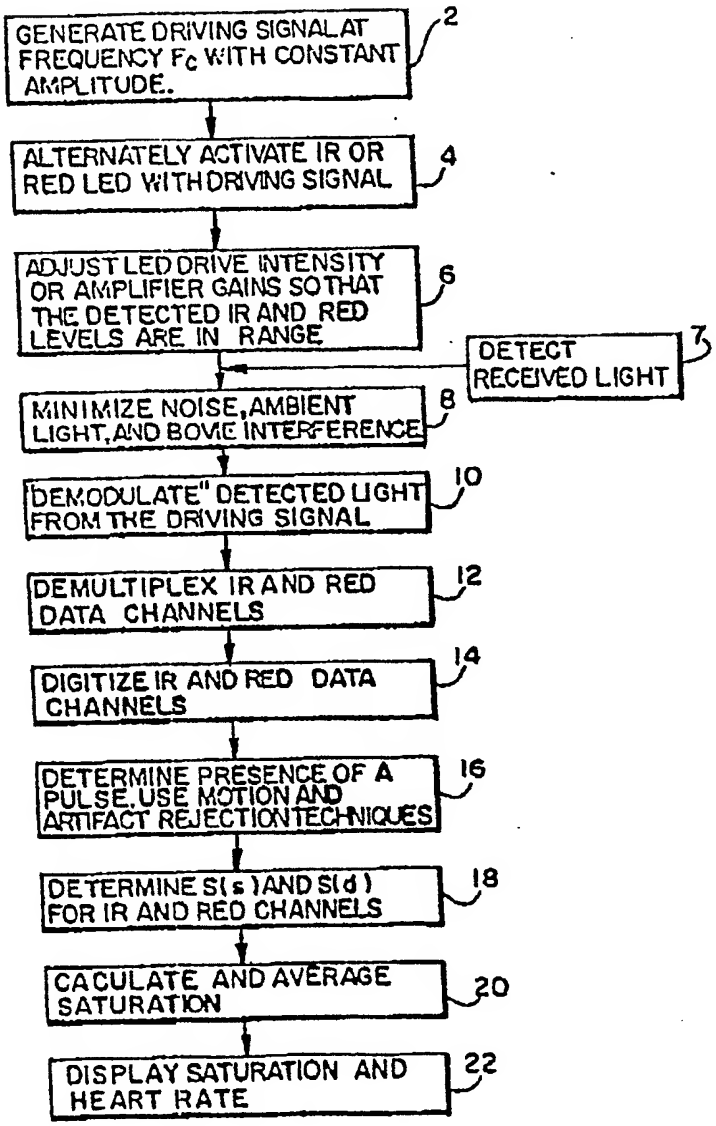

FIG. 1

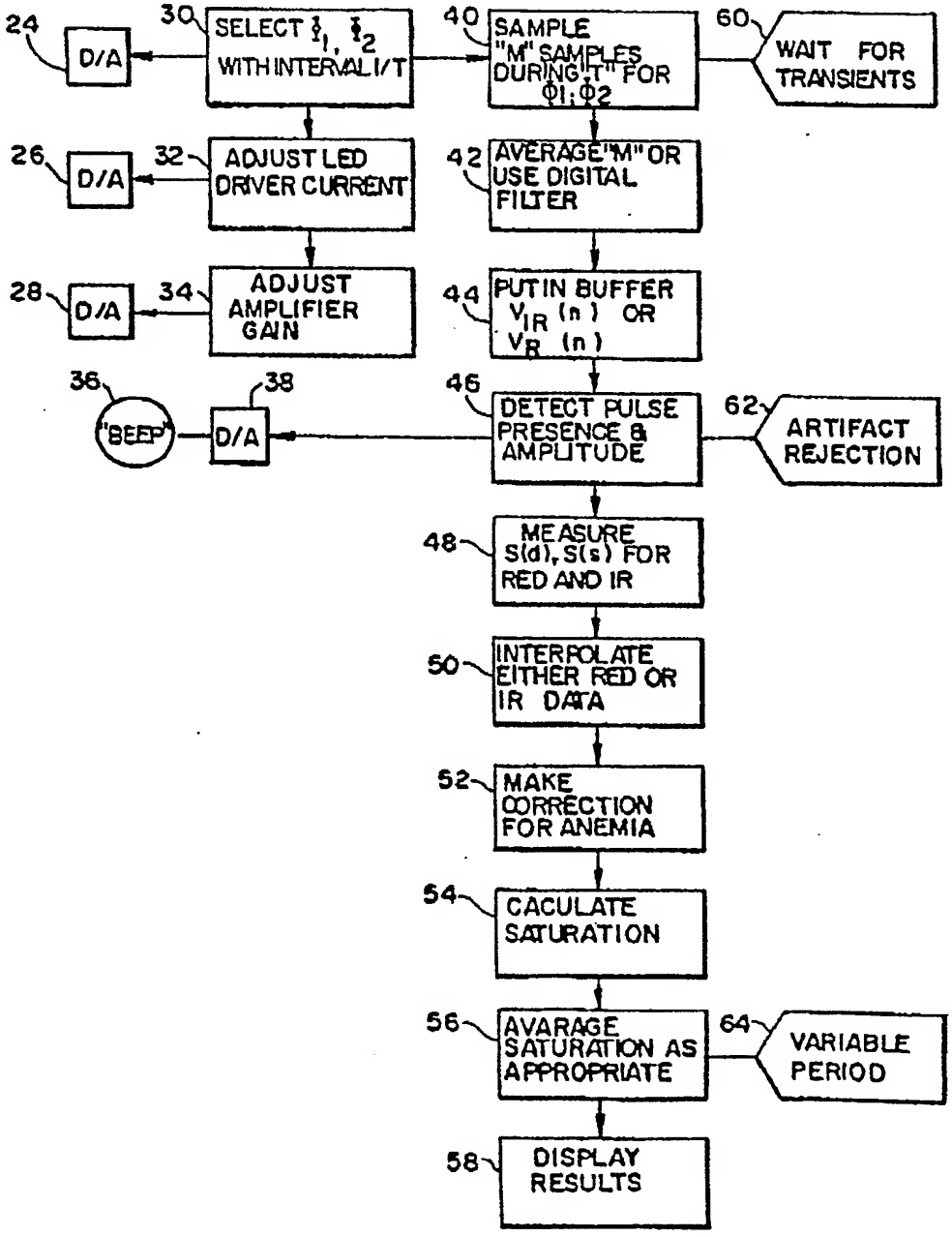

FIG. 2

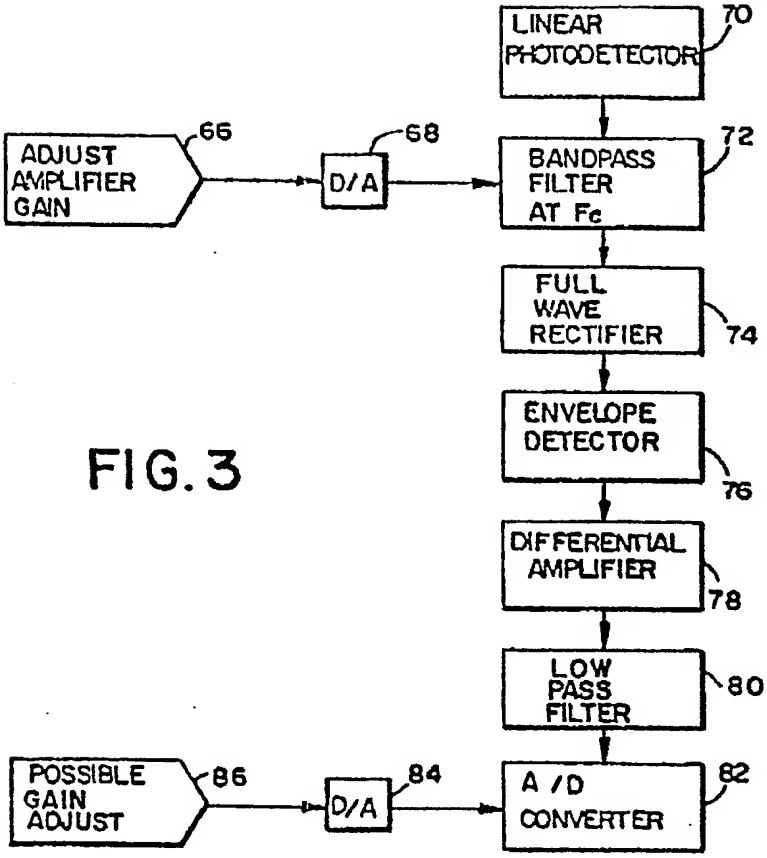
LINEAR PHOTODETECTOR
70
ADJUST AMPLIFIER GAIN
66
D/A
68
BANDPASS FILTER AT Fc
72
FULL WAVE RECTIFIER
74
ENVELOPE DETECTOR
76
DIFFERENTIAL AMPLIFIER
78
LOW PASS FILTER
80
POSSIBLE GAIN ADJUST
86
D/A
84
A/D CONVERTER
82

FIG. 3

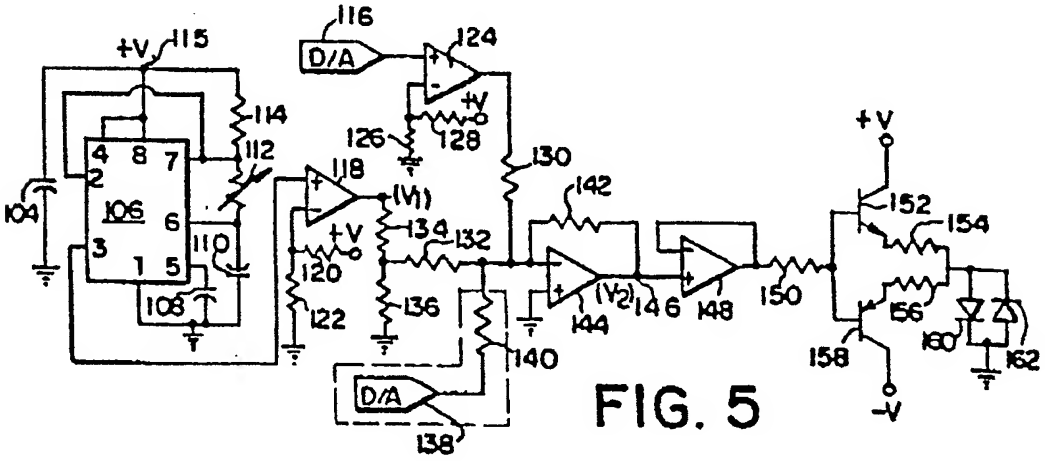
+V
115
116
D/A
124
114
112
126
128
130
118
(V1)
142
104
106
134
132
110
120
152
154
122
136
144
146
148
150
156
140
158
160
162
D/A
138
-V

FIG. 5

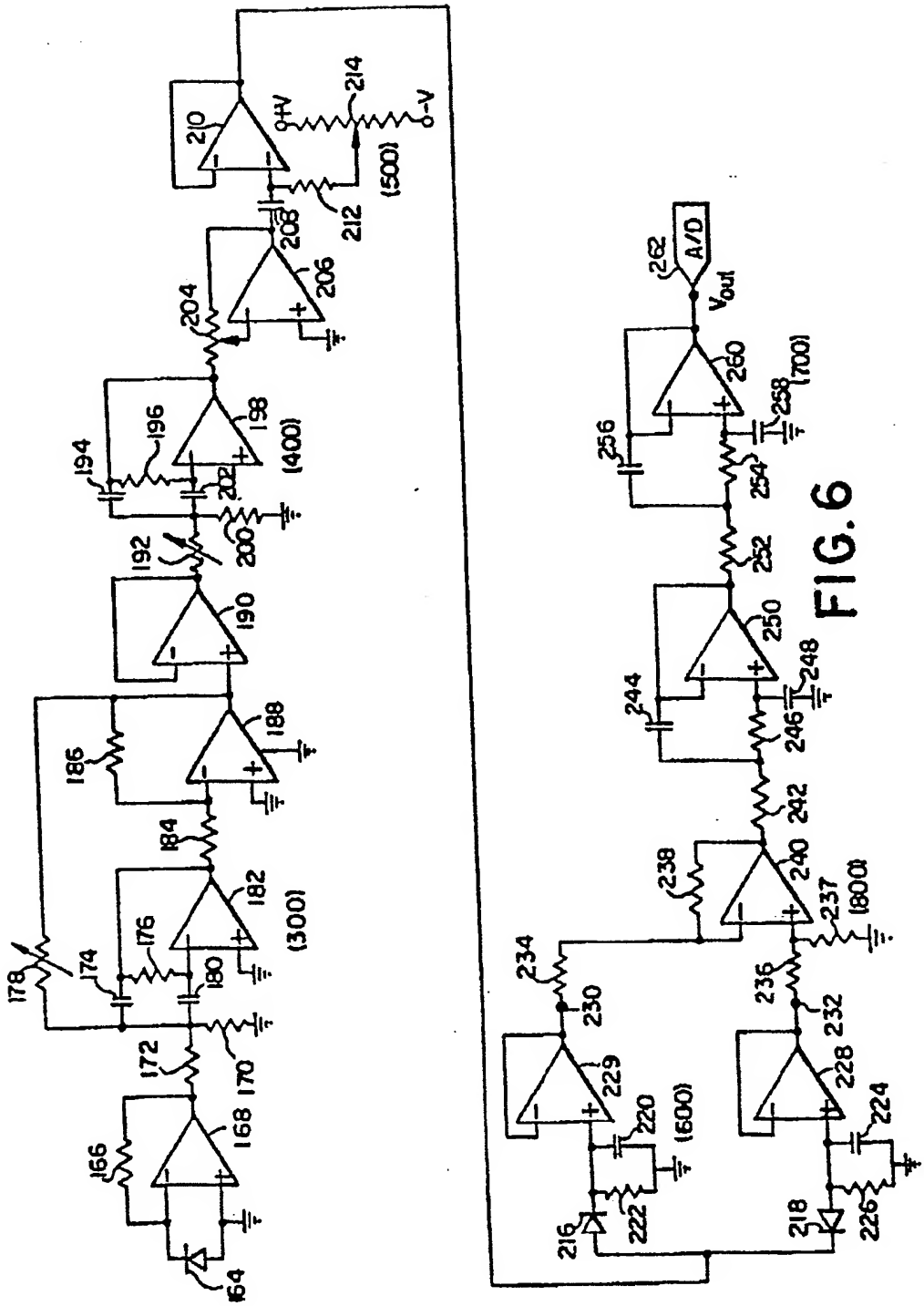

FIG. 6

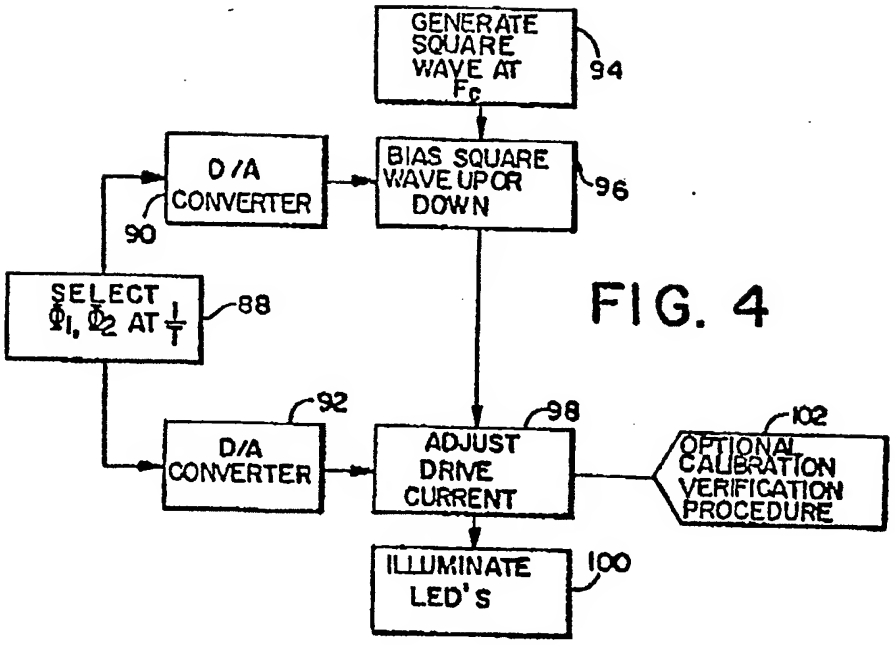
GENERATE SQUARE WAVE AT Fc
94
BIAS SQUARE WAVE UP OR DOWN
96
D/A CONVERTER
90
SELECT Φ1, Φ2 AT 1/T
88
D/A CONVERTER
92
ADJUST DRIVE CURRENT
98
OPTIONAL CALIBRATION VERIFICATION PROCEDURE
102
ILLUMINATE LED'S
100

FIG. 4

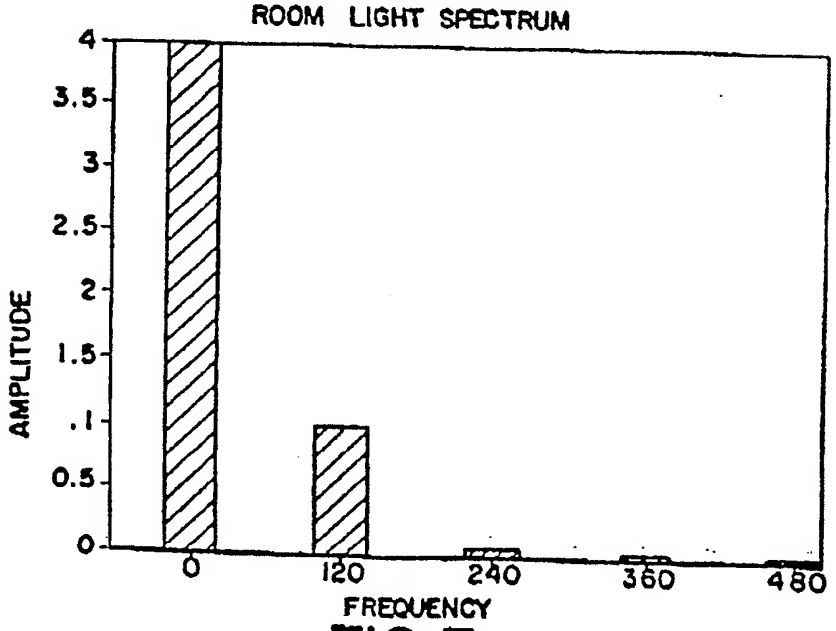
ROOM LIGHT SPECTRUM
AMPLITUDE
4
3.5
3
2.5
2
1.5
.1
0.5
0
0
120
240
360
480
FREQUENCY

FIG. 7

European Patent Office

EUROPEAN SEARCH REPORT

Application Number

EP 87 31 0869

DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int. Cl.4)
Y	MEDICAL AND BIOLOGICAL ENGINEERING, vol. 10, no. 1, January 1972, pages 9-22, Pergamon Press, GB; F.J. JANSSEN: "The principle design and features of a new Hb-oximeter" * Abstract; page 15, "Photometer and electronics"; figure 4 *	1-10	A 61 B 5/00
Y	EP-A-0 160 768 (BATTELLE MEMORIAL INSTITUTE) * Page 8, line 7 - page 9, line 34; figures 1,3 *	1-10	
A	DE-A-2 136 823 (F. HELLIGE & CO. GmbH) * Whole document *	1,3	
A	US-A-3 463 142 (HARTE) * Abstract; column 3, line 19 - column 4, line 69; figures 2,3 *	1,3	
A	US-A-4 555 179 (LANGERHOLE et al.) * Column 7, lines 15-56; column 9, lines 5-17; figure 5 *	1,2,5,6	TECHNICAL FIELDS SEARCHED (Int. Cl.4)
A	WO-A-8 600 514 (JOHN HOPKINS UNIVERSITY) * Page 18, line 16 - page 20, line 12; claim 37; figure 5 *	1,3-6	A 61 B

The present search report has been drawn up for all claims

Place of search	Date of completion of the search	Examiner
THE HAGUE	25-02-1988	CHOWDHURY

CATEGORY OF CITED DOCUMENTS

X : particularly relevant if taken alone
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A : technological background
O : non-written disclosure
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T : theory or principle underlying the invention
E : earlier patent document, but published on, or after the filing date
D : document cited in the application
L : document cited for other reasons

& : member of the same patent family, corresponding document

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